show an abnormal reaction. The other tests were done on the knees, which had previously been the sites of lesions; but the fact that they had been kept covered may explain the loss of sensitiveness.

The porphyrinuria present in the second case is of particular interest in that it was formerly thought that the porphyrins were photosensitizers and that their presence was the determining factor in the development of hydroa-like eruptions, even though they were demonstrable in less than half of the cases. Schreus and Carrié pointed out that a number of authors consider that the presence of porphyrins in the urine in considerable amounts indicates a congenital porphyrinuria which may be associated with light sensitiveness. This light sensitiveness is not true hydroa, according to this group. In the past few years the opinion has gained ground that porphyrinuria was the result of changes which occurred as a result of exposure to the sun.

384 Post Street.

TUBERCULOUS CAVITIES—THEIR SIGNIFICANCE, PROGNOSIS AND TREATMENT*

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DISCUSSION *by Robert A. Peers, M.D., Colfax; F. M. Pottenger, M.D., Monrovia; Philip H. Pierson, M.D., San Francisco.*

IN 1921 Graff [1] stated that the tuberculous cavity is the death sentence for its bearer.

Pinner,[1] too, says: "Cavities are, of course, compatible with long periods of life; but, barring intercurrent disease, their bearers will eventually die from causes more or less directly attributable to the cavity." In the face of these striking statements, a study of the situation seems worth while.

CLINICAL TUBERCULOSIS AN ALLERGIC PHENOMENON

Clinical tuberculosis is an allergic phenomenon. The inflammatory reaction and the symptoms of toxemia are primarily a reaction by the tissues to the bacterial proteins. The entrance of the tubercle bacillus into the tissues of an individual who has not experienced a previous infection excites only a mild nonspecific inflammatory reaction, followed by destruction or encapsulation of the organism.

This is simply the response of the tissues to the presence of a foreign body. In the course of three or four weeks the tissues become allergic, and an acute inflammatory reaction is set up. In the already allergic individual—and the large majority of adults come within this category—the inflammatory reaction is prompt and vigorous, varying in intensity according to the degree of allergy possessed by the individual and the amount of bacterial protein—antigen—present. The virulence of the bacilli has always been considered to be an essential factor, but the recent work of Bogen [2] suggests that this may play a much smaller rôle than we have thought. Differences in the chemistry of the tissues of different individuals, or of the same person at different times, undoubtedly play a part, though the substances concerned are as yet largely unknown.

This allergic response is of two types—exudative and proliferative. In the exudative type the reaction is acute, with extensive exudation. In the proliferative type it is more chronic, with a strong tendency to the formation of fibrous tissue. Cases are classified as exudative or proliferative, depending upon which phenomenon predominates in the lesion, but both processes may be and usually are present at the same time in different portions of the areas involved.

EXUDATIVE TYPE

The exudative type is distinguished by the acuteness of the inflammatory reaction about the focus of infection. The pulmonary alveoli in the area immediately surrounding the bacilli are filled with an inflammatory exudate—the allergic response to the tubercle toxins† rather than to the presence of the bacilli themselves.

We have, then, a central area, more or less well defined, containing the tubercle bacilli and the epithelioid cells, round cells, etc., which go to make up the tubercle proper. Surrounding this is a more or less extensive area of collateral inflammation—pneumonitis. As encapsulation of the bacilli proceeds, with limitation of the circulation of toxic products, this collateral inflammation tends to subside, and absorption of the exudate takes place as in lobar or bronchopneumonia, though much more slowly. Its retrogression can be clearly seen if serial roentgenograms are taken at suitable intervals.

In the center of these areas, where the bacilli are present in the greatest numbers, the concentration of toxic bacillary products may be sufficient to cause necrosis. This occurs in most cases of tubercle formation. The individual tubercle covers an extremely small area; and if the process is confined to localized tubercle formation, comparatively little damage is done. But unfortunately this is not always the case, and larger areas of necrosis frequently develop. Whether this is by a gradual enlargement of the initial necrotic area, as takes place in an ordinary furuncle, or a fusion of contiguous enlarging tubercles comparable to carbuncle formation, is not material to this discussion.

As the necrotic tissue liquefies, it is only required that rupture and evacuation into a bronchus occur. We then have definite cavity formation. Strictly speaking, the evacuation of a single tubercle constitutes cavity formation, but for practical purposes we limit the term to areas large enough to be seen on the x-ray film.

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† The term, "tubercle toxins," is loosely used to designate the products of tubercle bacilli. No true toxins ever have been demonstrated. The products of the tubercle bacillus are toxic only after allergy to them has been developed; that is, they are toxic only to the allergic individual.

TABLE 1.—*Results in Pulmonary Cavities at the End of Six Years*

CAVITIES—6 YEARS							
	Total	Arrested	Quiescent	Improved	Unimproved	Worse	Dead
Under 1.5 inches	7	0	2	1	0	3	1
1.5 to 2.5 inches	15	2	2	3	0	2	6
Over 2.5 inches	10	0	0	2	0	1	7
Multiple	6	0	0	2	0	1	3
Total	38	2	4	8	0	7	17
Per cent	100	5	10	21	0	18	45

These cavities are "acute" cavities. They may be of any size and of any shape, but are usually not very large; and they form in the early weeks or months following the onset of the disease, or during an exacerbation. They are surrounded by a somewhat irregular wall of infiltration containing relatively little fibrous tissue.

PROLIFERATIVE TYPE

In the proliferative type of tuberculosis, as has already been noted, fibrous tissue formation is the predominating phenomenon. The process is essentially a chronic one. It may have been going on for many months or even years. The tissues are allergic, but they also possess a high degree of tolerance to the bacillary products. A high degree of immunity is present, but not quite sufficient to arrest the progress of the infection. In the presence of this fibrous tissue a concentration of toxins sufficient to cause necrosis is finally reached, and a cavity formed. Usually this cavity has been present for some time before the patient is seen by the physician. Its wall contains much fibrous tissue, and in consequence is more or less rigid. The fibrous tissue in the adjacent areas renders those portions of the lung much less elastic than normal. Because of the long duration of the disease, we are apt to find pleural adhesions, fixed mediastinum, etc.

SIGNIFICANCE

In general we may say, therefore, that cavity formation indicates an intense infection in that portion of the lung. It indicates, also, a degree of immunity which enables the tissues to localize the infection rather than to permit its dissemination throughout the lung. It is analogous to the difference between pyogenic abscess and septicemia.

PROGNOSIS

The time is not long past since the general opinion was, once a cavity, always a cavity. The taking of serial roentgenograms of patients, however, has demonstrated beyond question that cavities, particularly acute cavities having a spheroidal outline, can and frequently do heal, becoming obliterated and leaving only a small amount of fibrous tissue to indicate their former existence.

The cavity which is not healed usually continues to throw off tubercle bacilli. Exceptionally, the wall may heal to a smooth inner lining of fibrous tissue, but in most cases activity persists to a greater or less degree. For this reason, unhealed cavities constitute a very definite menace to the future health of the individual. Numerous studies have been made to determine the extent of this danger.

Kötter [3] states that clinical healing of cavities occurs in 15 per cent of cases. Sprungmann [4] says that two years after taking the cure 61.7 per cent of cavity patients were dead, and in five years 75.7 per cent.

Barnes and Barnes,[5] in a study of 1,454 cavity cases, found that, at the end of one year after diagnosis, 80 per cent of the patients were dead, and at the end of five years 90 per cent had died.

Head, Schlack, and Marx [6] (Table 1) followed thirty-eight patients with cavities over a period of six years, and found that at the end of that time 45 per cent were dead and 18 per cent worse, and that only 5 per cent could be considered arrested and 10 per cent quiescent. Their figures also indicate that the smaller the cavity, the better the prognosis.

Fales and Beaudet,[7] of the U. S. Veterans' Bureau, in a study of 147 patients with cavity formation (Table 2), observed over a period of twenty-four months, found that a total of 62 (42 per cent) had healed.

Their figures show that, of the cavities occurring in cases with minimal involvement, two out of three healed. These, of course, were small

TABLE 2.—*Results in Pulmonary Cavities at the End of Twenty-four Months*

CAVITIES—24 MONTHS									
	Minimal		M. A.		F. A.		Total		Per Cent Healed
	Number	Healed	Number	Healed	Number	Healed	Number	Healed	
Under 2.5 cm.	3	2	32	23	21	12	56	37	66
2.5 cm. or over	..	..	15	7	29	3	44	10	23
Multiple	..	..	8	4	39	11	47	15	32
Total	3	2	55	34	89	26	147	62	42
Healed	66 per cent		62 per cent		30 per cent				

cavities. In 55 moderately advanced cases, 34 (62 per cent) of the cavities were healed after two years of more or less continuous rest, while of 89 far-advanced cases only 26 (30 per cent) were healed. When the cavities are classified as to size, it is seen that of those under 2.5 centimeters in diameter, 55 per cent healed, while only 23 per cent of the cavities larger than that, and 32 per cent of the multiple cavities, healed.

These are easily the most favorable results reported in a series of this size, and it is a striking demonstration of what can be accomplished by persistence. In dealing with private patients, however, one cannot but feel that twenty-four months is rather long to wait before concluding that a cavity requires more active treatment.

All these statistics, of course, refer to patients who received only conservative treatment. Obviously, Graff's statement that the tuberculous cavity is the death sentence for its bearer is applicable only to medium-sized and large cavities, that is, cavities having a diameter of two or three centimeters, which do not receive surgical treatment. It *is* evident, however, that an open cavity seriously complicates the prognosis, and that the gravity of this complication is roughly proportionate to the number and size of the cavities present.

TREATMENT

In justice to the patient, therefore, every reasonable means must be used to secure the healing of any cavities which may be present. These means will, of course, vary to some extent with the conditions found in the particular case under consideration. With rare exceptions conservative measures should be given a fair trial. When they fail, some form of collapse therapy is indicated.

The simplest procedure and the one carrying the least risk for the patient is pneumothorax, the lung being slowly collapsed and the collapse maintained for a period of two to four years in the average case. The perfection of the technique for the induction and maintenance of pneumothorax, and the popularization of the operation, may fairly be considered the greatest single advance in the treatment of tuberculosis in the past generation. There is no more spectacular result in the entire field of medicine and surgery than that obtained by a successful pneumothorax in a very ill patient.

A plan of procedure applicable to most cases with cavities may be outlined as follows:

As soon as the diagnosis is made, the patient is immediately placed on bed rest. If he is able to use the bedpan without undue strain — and many are not—he remains absolutely in bed. If not, and his strength permits, he is allowed to go to the bathroom for bowel movements. A fair proportion of patients with early and more or less acute lesions will respond promptly with a diminution in temperature and pulse rate, the former frequently becoming normal in from within a few days to a week or two. Cough and expectoration show a corresponding improvement, though some expectoration usually persists for a considerable period. At the end of three to six weeks (the time depending somewhat upon the extent and acuteness of the lesion), stereoscopic roentgenograms are taken, by portable apparatus if necessary. If the cavity is getting smaller, the program is continued and another picture made in six weeks to two months. As long as the cavity is diminishing, no radical measures are indicated. It is surprising and gratifying to see the rapidity with which this can take place at times; frequently it will continue to obliteration, the patient becoming practically symptom-free and usually showing a substantial gain in weight.

A word of warning is in order in dealing with these favorable cases from this time forward. While exercise may be carefully increased, this increase must be carried out very slowly, and particular care taken to protect against acute respiratory infections, because a comparatively slight degree of overexercise, or a severe cold, may cause a softening of the fibrous tissue and a reestablishment of the cavity with startling rapidity. If these pitfalls are avoided, the ultimate result is most excellent, because, along with the disappearance of the cavity, there will be a considerable degree of resolution in the surrounding portions of the lung. The ultimate amount of fibrous tissue is usually surprisingly small as compared with the amount of involvement originally present.

When the patient does not respond to a strict rest program, and the symptoms fail to show a reasonable degree of amelioration, the second roentgenogram will usually fail to reveal improvement in the lesion, and may show progression. Depending upon the extent and activity of the lesion and the estimated risk of extension, particularly to the other lung, collapse therapy may be indicated at this time, or one may temporize for another month. The longer one waits, the greater is the risk of the formation of pleural adhesions which will render collapse impossible by any measures short of thoracoplasty. I have more frequently regretted postponing pneumothorax than inducing it too soon.

Chronic cavities, because of the fibrous tissue present in their walls, frequently require a somewhat different procedure. In some cases also, one will find evidence of beginning complications, such as extension of the infection into the better lung, which call for immediate intervention. For reasons not yet fully understood, the clover-leaf type of cavity (usually acute) shows a marked tendency to enlarge rather than heal under conservative treatment. In such cases, and in the absence of contraindications, therapeutic pneumothorax is attempted.

Unfortunately, because of pleural adhesions, it is impossible to secure free pleural space in approximately one-third of the cases and, for these, more radical measures have to be considered. Sometimes a simple exairesis of the phrenic nerve suffices. Section and avulsion of the phrenic nerve supplying the diaphragm on the affected side is a minor operation, so far as shock to the patient is concerned, though not free from occasional serious and even fatal complications. The resultant paralysis of the diaphragm puts a stop to the

downward pull on the lung with each inspiration, and to that extent reduces pulmonary activity. Because of the positive intra-abdominal pressure and the negative intrapulmonary pressure, the paralyzed and relaxed diaphragm tends to rise, reducing the volume of that half of the thorax by from 15 to 30 per cent. The resultant relaxation of the lung exercises a salutary effect upon the lesions situated in the lower portion, and frequently is of great benefit to those in the upper portion, even as high as the apex.

It may not be amiss to sound a word of warning to the surgeon who is impressed by the apparent simplicity of the operation. The phrenic nerve presents definite anomalies in over 30 per cent of cases. The occasional persistence of diaphragmatic motility, and the not rare development of ptosis and permanent pupillary dilatation, attest to the pitfalls the operation affords for the unwary.

If the disease is extensive and practically unilateral, or if the cavity is large, thoracoplasty may have to be considered. We venture the hope that some of the partial thoracoplastic operations which are now being developed by the thoracic surgeons may prove satisfactory for apical lesions and so enable us to conserve the greater part of the functioning pulmonary tissue in the remaining portion of the lung.

Occasionally pneumothorax is induced, but adhesions prevent a sufficient degree of collapse of the more severely diseased portions of the lung to secure a satisfactory result. In time, many of these stretch sufficiently. If they do not, and they are very dense, it may be necessary to resort to thoracoplasty. In a few cases they are so small and thin that they may be severed by the cautery (intrapleural pneumolysis), using an instrument somewhat similar to the cystoscope. There is danger of cutting through a blood vessel with resultant serious or fatal hemorrhage, or severing a tongue of pulmonary tissue drawn out into the adhesion, with consequent infection of the pleura and empyema of a malignant type. In skilled hands this seldom occurs, but the operation is one calling for a high degree of technical ability.

A judicious selection, and use of these methods which modern medical science has placed at our disposal, will not only help us to a more optimistic attitude toward the tuberculous patient, but will enable us to shorten the convalescent period and restore many more of these unfortunates to health and economic independence.

SUMMARY

1. Cavities constitute a serious complication of a pulmonary tuberculous process.

2. Their persistence means, in most cases, a relatively short expectation of life.

3. A trial of conservative measures should usually be made.

4. If unsuccessful, we should not hesitate to have recourse to collapse therapy.

5. Too much time should not be lost before considering the means to this end.

307 West Eighth Street.

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DISCUSSION

ROBERT A. PEERS, M. D. (Colfax).—Doctor Howson gives in concise, easily understood language a clear picture of the pathology of tuberculosis as viewed in the light of recent studies in allergy as related to tuberculous infection. He has traced briefly and lucidly what happens in both the exudative and proliferative types of pulmonary tuberculosis. He reviews the mechanism of cavity formation, the potential danger of cavities, and the pessimism of many writers in discussing the prognosis in patients with cavity formation.

All of this is important, but what strikes the writer, in reviewing Doctor Howson's paper, is his common sense, conservative but at the same time complete, method of attack in the treatment of cavity. He agrees as to the gravity of cavity formation, especially large-sized cavity, but he also recognizes that cavities, sometimes quite large cavities, heal spontaneously if given rest and time. He acknowledges, too, that there are cavities which rest and time alone will not heal, and which must be vigorously attacked by pneumothorax, by the intrathoracic severing of adhesions, by phrenic exairesis, by thoracoplasty or other surgical methods.

Everyone of experience, who has watched his patients closely over a considerable period of time with serial x-rays or fluoroscopic screenings, will bear witness to the truth of Doctor Howson's presentation. He will see fairly large cavities become smaller and smaller, finally disappearing and leaving, as Doctor Howson has stated, "only a small amount of fibrous tissue to indicate their former existence." And with this experience in mind he becomes conservative. Again, he will see in other patients with apparently similar involvement the increase in size of cavity and/or the spread of disease, and he will recognize that delay is no longer conservatism, but procrastination. The writer thinks that we all have felt, to quote again: "I have more frequently regretted postponing pneumothorax than inducing it too soon."

That some cavities will heal spontaneously, is certain. That some others will not do so is also certain. That the prognosis in every case of cavity is not gloomy, is also certain. That upon the skill and judgment of the attending physician depends largely the prognosis, is certain. The ability to know when to be conservative and when to invoke surgical measures is an expression of the possession of what is known as "art in medicine."

F. M. POTTENGER, M. D. (Monrovia).—It is refreshing to hear an optimistic paper regarding tuberculous cavities. I have long contended that the usual pessimistic attitude toward the healing of tuberculous cavities is wrong. It is not based on an understanding

of either tuberculosis or the intrathoracic mechanics. Too many of the reports which have been published in the past have been recitations of the final outcome of patients who had destructive lesions in the lung, rather than descriptions of the results following the intelligent treatment of cavities when all conditions which favor or hinder healing have been taken into consideration.

I pointed out some time ago, in a paper which appeared in the *American Review of Tuberculosis,* that the two principal factors in the healing of tuberculosis are the resistance of the patient, both natural and specific, and the intrathoracic mechanics; and further pointed out that in early simple lesions resistance is most important, while in advanced and far advanced cases intrathoracic mechanics are often of greater importance, because resistance may be satisfactory, but healing is prevented by mechanical obstacles, such as fibrosis, adherent pleura, fixed mediastinum, and widespread emphysema.

It has been my experience that a large percentage of acute cavities, particularly in patients suffering from predominantly exudative tuberculosis, will heal without surgical interference. The reason for this is that most of the conditions which are favorable to healing are present. The patient's health, as a rule, has not been undermined by long illness; as a rule the pleura is free, the mediastinum is movable; and the pulmonary tissues outside of the area of involvement are elastic and able to take on the amount of compensatory emphysema necessary to compensate for the loss produced by the cavity.

I have found that the usual regimen of rest, hygienic living, good food, assisted by shot bags over the infected area to lessen the motion, have been sufficient to bring about healing in nearly all cases of this type.

In cavities which appear in chronic proliferative tuberculosis, the healing is not so easy because, as a rule, in this type there has been more or less interference with the factors favorable to compensation. The lesion is proliferative, consequently the tissues are not so elastic; pleural adhesions are more apt to be present; the mediastinum is more apt to be fixed, and compensatory emphysema in many of these cases has already taken place to a greater or lesser degree. In spite of this many fresh cavities in lesions predominantly proliferative will heal.

In the chronic cavity surrounded by a dense fibrous wall, healing rarely occurs under a noninterference policy, because no matter how high the immunity the necessary compensation is interfered with.

In summing up our experience, I would say:

1. An acute cavity in a lesion predominantly exudative will nearly always heal unless it be well up in an apex which is covered with a pleural cap, or close to the hilum, where the tissues are very dense.

2. An acute cavity in chronic proliferative tuberculosis will heal in a much smaller percentage of cases, because of interference with the various mechanical factors.

3. Cavities with dense fibrous walls will rarely heal without the aid of some form of compression.

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PHILIP H. PIERSON, M. D. (490 Post Street, San Francisco).—Doctor Howson's paper presents clearly and concisely important facts that bear emphasis. The treatment, when a cavity is present, is much more likely to succeed if the cavity has but recently developed, and for two reasons: (1) in time, epithelium may grow from a neighboring bronchus and cover the inner wall, making subsequent adhesion of the walls impossible when any form of collapse therapy is instituted; and (2) a thin-walled cavity disappears by, first, the absorption of this walling-off membrane, and then dilation of the surrounding alveoli.

I agree that generally there should be a waiting period after the patient is put to bed at absolute rest, for Nature has often shown herself to be very helpful if given a chance. If no improvement is evident in the cavity in three months, interference should be considered. If we are dealing with bilateral disease with the cavity on only one side, a longer delay may be in order, for the picture is considerably complicated by the manifest disease in the contralateral lung.

The length of time pneumothorax must be continued is a difficult question to answer. A treatment which is succeeding in keeping the patient well may be a good one to continue for more than two to four years.

A small adhesion which is holding open a cavity may be burned by cautery. I saw Doctor Jessen deal with a broad band by removing a section of the two overlying ribs, and then pneumothorax was adequate.

Where apical cavities are adherent, so that pneumothorax is unsuccessful, I doubt that phrenectomy will benefit; but with subclavicular ones this procedure is helpful at times. The complete excision of the upper three ribs and a portion of one or two more posteriorly, has been successful in a small series, and it has saved for the patient his relatively good lower lobe, much of which would have been sacrificed by phrenectomy.

PREGNANCY AS A COMPLICATION OF HEART DISEASE*

By INA M. RICHTER, M. D.
AND
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DISCUSSION *by Saxton T. Pope, Jr., M. D., San Francisco; Alice F. Maxwell, M. D., San Francisco; William J. Kerr, M. D., San Francisco.*

THE effect of pregnancy on women with abnormal cardiac mechanism has been widely studied, especially during the last ten to fifteen years. Certain facts of the relationship have been rather satisfactorily established: that for women with certain types of heart disease pregnancy brings an additional risk; that cesarean section is the safest method of delivery for patients with decompensation; and that local anesthesia is preferable to general, except for the hyperemotional patient. Not yet so well established are the following points which we would suggest for further investigation: the diagnostic differentiation of patients with organic lesions from those showing abnormal signs and symptoms wrongly attributed to cardiac disease; the functional capacity of the myocardium in organic lesions in especial reference to the comparative value of frequent periodic observation versus exercise tests; and the effect of an inadequate cardiovascular system on the fetus.

CLINICAL MATERIAL FOR THIS STUDY

Our group of eighty-six pregnant women was referred by the department of obstetrics of the University of California Hospital and studied in the Cardiac Clinic of the same institution. The patients were seen every two to four weeks during pregnancy, and again postpartum wherever

* From the department of medicine, University of California Medical School.

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